REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. The amendments to the claims are supported in the specification as follows: p.6, lines 2-5; p.6, lines 15-16; p.6, lines 24-27; p.7; 26; p.7, lines 1-2; p.7, line 33 to p.8, line 9; p.8, line 20 to p.10, line 2; p.13, line 9 to p.16, line 8, p.3, lines 20-23; p.3, line 35 to p.4, line 6; p.5, lines 31-34; p.6, lines 2-5; p.6, lines 15-16; p.6, lines 24-27; p.7; 26; p.7, lines 1-2; p.7, line 33 to p.8, line 9; p.8, line 20 to p.10, line 2; p.13, line 9 to p.16, line 8.

Priority Documents

As confirmed by the Notice of Acceptance dated March 4, 2004, the USPTO has received the priority document. The Examiner, however, in the Office Action Summary, did not check the box indicating that the priority document has been received. Accordingly, acknowledgement of receipt of the certified copy of the priority document is respectfully requested in the next communication from the Examiner.

Moreover, applicants submit that the proper priority date for the present application is August 20, 1998, which is the priority dated recognized by the USPTO on the Notice of Acceptance.

IDS

An IDS was filed on January 5, 2005, disclosing three references that were cited in a counterpart foreign application. The Examiner is respectfully requested to return an initialed copy of the related SB-08 with the next communication.

Drawings

The Examiner has not yet indicated in the Office Action Summary that the drawings filed with the original application papers on February 20, 2001 have been accepted. Acceptance of these drawings is respectfully requested in the next communication from the Examiner.

Rejections Under 35 USC § 101, Utility

Claim 9 stands rejected due to a lack of utility. The Examiner has alleged that none of the blood cells as defined expresses FLT3/ITD. Claim 9 has been amended to overcome this rejection.

Rejections Under 35 USC § 112, First Paragraph, Enablement

The examined claims stand rejected for lack of enablement. Amended claim 1 is now directed to "a drug to treat blood cancer" and by screening "blood cells or hematopoietic stem cells". Applicants urge that in light of the disclosure of the specification the amended claims can be practiced without undue burden and therefore overcome the rejection for lack of enablement. One of ordinary skill in the art, in light of the teachings of the specification, would be able to experiment with the present invention to determine its effectiveness in screening "blood cells or hematopoietic stem cells" to find "a drug to treat blood cancer."

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation" MPEP § 2164, quoting from *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 UPSPQ2d 1217, 1223 (Fed. Cir. 1988). "The test of enablement is not whether experimentation is necessary, but whether, if experimentation is necessary, it is undue." MPEP § 2164, quoting from *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). (Emphasis added). Applicants contend, that under the guidelines of *In re Wands*, 8583 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), it would not require undue experimentation to carry out the invention of the present invention. One could follow the specification and conduct the appropriate assays to determine the effectiveness of the present invention.

Rejections Under 35 USC § 112, First Paragraph, Written Description and Enablement

Claim 9 has been rejected by reason that it is unclear if the cell lines, FDC-P1, 32D and BaF, are known and publicly available.

It is noted that cell lines FDC-P1, 32D and BaF were obtained from the publicly available cell banks and were not deposited by the applicants. Any person can access these cell lines. This is described in the specification page 7, lines 28-32. The FDC-P1 cell line is available from ATCC (American Type Culture Collection, P.O.Box 1549, Manassas, VA 20108, USA), Accession No. CRL-12103. The 32D and Ba/F3 cell lines are available from Cell Bank, RIKEN BioResource Center (3-1-1 Koyadai, Tsukuba, Ibaraki, 305-0074, Japan) with the Accession Nos. RCB 1145 and RCB 0805, respectively. Because these cell lines are available to the public, the rejection of claim 9 for lack of written description and enablement is improper and should be withdrawn.

Rejections Under 35 USC § 112, First Paragraph, Indefiniteness

Claim 1 has been amended to overcome the rejection for indefiniteness.

Rejection Under 35 USC § 102(b), Anticipation

The examined claims stand rejected as being anticipated by Lemoli et al (Blood, 1991, 77: 1829-1836) as evidenced by Kiyoi et al (Leukemia, 1998, 12: 133-1337) or Teller et al (Leukemia, 2002, 16: 1528-1534).

The Examiner has alleged that Lemoli et al teaches a method for screening a candidate compound for an antitumor drug, wherein said candidate compounds are Mab195 and 4HC comprising primary AML cells, contacting said cells with Mab195 or 4HC and culturing said cells in the absence of cytokines, detecting the proliferation of said cells and selecting a compound that inhibits the proliferation of said cells (see p.1831, columns 1 and 2, and Figure 2). She has also asserted that, although the reference does not specifically teach that the animal cells show cytokine-independent proliferation due to expression of FLT3/ITD, given the teaching of both Kiyoi et al and Teller et al that approximately 20% of AML patients present with FLT3/ITD it would be expected that at least a subset of the primary cells tested presented with FLT3/ITD and were therefore cytokine independent. Applicants strongly disagree with this position for the reasons that follow.

In order to more clearly distinguish the present invention from the Lemoli reference, step (d) of claim 1 has been amended to define that such inhibition of the proliferation of the cells is due to the inhibition of FLT3/ITD function.

As the left and right columns under the Abstract on page 1829 describe and Figure 2 on page 1931 specifically shows, what Lemoli et al tested to demonstrate is a cytotoxic activity of (i) MoAbs alone (anti-CD33 monoclonal antibody, M195, and anti-CD13 monoclonal antibody, F23), (ii) a chemical compound, 4-HC, alone, (iii) 4HC and VP16 (also chemical compound) in combination, and (iv) MoAbs, 4HC and VP16 in combination against myeloid leukemic progenitor cells (colony forming unit-leukemic; CFU-L) from an AML patient. Due to the cytotoxic activity (i.e., tumor lytic activity, tumor killing activity) of the agents, they purge the tumor cells that contaminate human bone marrow cells. This allows the bone marrow cells to be autologously transplanted (reinfused) to the AML patient. The tumor cell contamination of reinfused bone marrow cells is a potential source of relapse in the AML patients.

A difference between the present invention and Lemoli is that the present invention identifies a compound having a cell proliferation-inhibiting activity of the blood cells or hematopoietic stem cells in which the FLT3/ITD gene has been introduced. In contrast, Lemoli evaluated a tumor cell killing activity of known purging agent(s). No cell proliferation is detected in the Lemoli reference, instead Lemoli detects a reduced tumor cell recovery due to the cell killing.

As Figure 2 on page 1831 shows, a strong purging effect, below the lower limit of detection, was observed if different agents were used in combination compared to each being used alone. Importantly, in all experiments, more than 90% of the leukemic cells, CFU-L, were killed (i.e., less than 10% of the cell recoveries were observed for any experiments, whereas 100% recovery for control.). As the Examiner has asserted, it is evidenced by Teller et al or Kiyoi et al that only approximately 20% of AML patients present with FLT3/ITD. Assuming, *arguendo*, that the purging agent(s) alone or in combination that Lemoli et al tested worked to kill the CFU-L tumor cells by modulating a function of the FLT3/ITD that might be expressed on about 20% of the cells, it can be concluded that 70% or more of the

CFU-L tumor cells (90% minus 20%) were killed by any other mechanism than a modulation of the function of FLT3/ITD. Accordingly, it is apparent that the tumor lysis observed with the purging agent(s) occurred through other mechanisms not related to FLT3/ITD. Therefore, applicants respectfully request that the rejection for anticipation be reconsidered and withdrawn.

Rejection Under 35 USC § 103, Obviousness

The examined claims stand rejected as being obvious over Lemoli et al (supra) as evidenced by Kiyoi et al (supra) or Teller et al (supra) in view of Yokota et al (Leukemia, 1997, 11: 1605-1609, IDS item).

As discussed in detail above, the Lemoli reference does not teach or suggest all of the elements of the present invention. Yokota et al do not remedy these deficiencies. Moreover, none of the cited references provide motivation for a skilled artisan to arrive at the present invention. Finally, there is no reasonable expectation of success of the modification or combination of the cited references. The instant obviousness rejection thus fails to meet all of the three criteria needed to establish a prima facie case of obviousness (MPEP 706.02(j) and 2143.01 through 2143.03) and applicants respectfully request that it be withdrawn.

Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of

papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 18, 2005

By _____

FOLEY & LARDNER LLP
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5143
Telephone: (202) 672-5300
Facsimile: (202) 672-5399

Matthew E. Mulkeen
Attorney for Applicants
Registration No. 44,250